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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,601	03/30/2005	Nobuhide Watanabe	234991	1607

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LEYDIG VOIT & MAYER, LTD  
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EXAMINER

AULAKH, CHARANJIT

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 08/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/529,601	WATANABE ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Charanjit S. Aulakh	1625	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☐ Responsive to communication(s) filed on \_\_\_\_.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-8 and 11-14 is/are pending in the application.  
     4a) Of the above claim(s) \_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1,2,8 and 11-14 is/are rejected.
- 7) ☒ Claim(s) 3-7 is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
     a) ☒ All    b) ☐ Some \* c) ☐ None of:  
         1. ☐ Certified copies of the priority documents have been received.  
         2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_.  
         3. ☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- \* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152)             |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date <u>6/27/05</u> . | 6) <input type="checkbox"/> Other: ____.  |

### **DETAILED ACTION**

1. According to a preliminary amendment filed on March 30, 2005, the applicants have canceled claims 9 and 10 and furthermore, have amended claims 3-8, 11 and 12.
2. Claims 1-8 and 11-14 are now pending in the application.

### ***Claim Rejections - 35 USC § 112***

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 11 and 12 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for treating osteoporosis and climacteric syndrome, does not reasonably provide enablement for treating breast cancer or prophylaxis of osteoporosis, climacteric syndrome and breast cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The following eight different factors (see *Ex parte Foreman*, 230 USPQ at 547; *Wands*, In re, 858.F. 2d 731, 8 USPQ 2d 1400, Fed. Cir. 1988) must be considered in order for the specification to be enabling for what is being claimed:

Quantity of experimentation necessary, the amount of direction or guidance provided, presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability and the breadth of claims. In the instant case, the specification is not enabling based on at least four of the above mentioned eight different factors such as quantity of experimentation

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necessary, the amount of direction or guidance provided, presence of working examples, the state of the prior art, unpredictability and the breadth of claims.

The specification teaches that the instant spiro compounds are estrogen receptor modulators. However, there is no teaching in the specification whether these spiro compounds are agonists or antagonists of estrogen receptors. The specification demonstrates the efficacy of instant compounds in animal models of climacteric syndrome ( see tables 1 and 2 on page 32 ) and osteoporosis ( bone density ) as shown in table 5 on page 35. Based on these data, the instant compounds will have utility in treating osteoporosis and climacteric syndrome. There are no working examples present showing efficacy of instant compounds in known in vitro or in vivo models of breast cancer. There is no guidance present how the instant compounds will have utility in treating breast cancer. There is no teaching either in the specification or prior art regarding well known utility of structurally closely related compounds in treating breast cancer. There is lot of unpredictability regarding therapeutic effects of estrogen receptor modulators on different functions as evidenced by the instant specification which mentions beneficial effect of known estrogen receptor modulators, raloxifene and tamoxifen on breast cancer and osteoporosis and actually aggravation of climacteric syndrome or hot flash ( see page 3, lines 10-17 ) whereas the instant compounds have efficacy in animal model of climacteric syndrome. The instant compounds of formula (I) encompasses hundreds of thousands of compounds based on the values of variables R1, R2, A and n and therefore, in absence of such teachings, guidance, presence of working examples and unpredictability, it would require undue experimentation to

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demonstrate the efficacy of instant compounds in known in vitro or in vivo models of breast cancer and hence their utility for treating breast cancer.

It is also well known in the art that multiple mechanisms are involved in the etiology of any known disease condition including osteoporosis, breast cancer and climacteric syndrome and therefore, correcting one of these several mechanisms will not completely cure ( prophylaxis ) that specific disease condition.

5. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

6. Claims 1, 2, 8 and 11-14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

In independent claim 1, formula (I), ( CH<sub>2</sub> )<sub>n</sub> appears to be outside the ring and not part of the ring.

In independent claim 1, for the value of variable A, formulae (a) and (c), (CH<sub>2</sub>)<sub>r</sub> appears to be outside the ring and not part of the ring.

In claim 13, in formula (II), it appears that ' is attached to the phenyl ring instead of variable A'.

In claim 13, for the value of variable A', formulae (a) and (c), (CH<sub>2</sub>)<sub>r</sub> appears to be outside the ring and not part of the ring.

In claim 14, formula (III), ( CH<sub>2</sub> )<sub>n</sub> appears to be outside the ring and not part of the ring.

***Allowable Subject Matter***


7. Claims 3-7 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

The instant compounds are allowable over the prior art since they are neither disclosed nor obvious over the prior art. In the prior art, Blizzard ( WO 02/091993, cited on applicants form 1449 ) discloses estrogen receptor modulators which are related to instant compounds. However, closely related compounds ( see pages 6-8 ) disclosed by Blizzard differ in structure from the instant compounds and furthermore, there is no teaching, guidance or motivation in the prior art to modify the compounds of Blizzard to prepare the instant compounds.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Charanjit S. Aulakh whose telephone number is (571)272-0678. The examiner can normally be reached on Monday through Friday, 8:30 A.M. to 5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Thomas McKenzie can be reached on (571)272-0670. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

  
Charanjit S. Aulakh  
Primary Examiner  
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